

The strengths and frailties of women with cardiovascular disease

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Shakespeare¹ and popular belief have tended to reinforce the view that females are weak. Scientific methodology applied to the field of cardiovascular disease suggests, to the contrary, that women are strong and enduring²⁻⁷. Compared to males, females live at least 4 years longer^{2,3}, develop ischemic heart disease about 10 years later⁴, require more risk factors before manifesting heart disease⁵, are less subject to sudden cardiac death⁶, and appear to have a more favorable outcome after the onset of heart failure⁷.

What gives women their strength? A first obvious candidate is the distinctive hormonal *milieu* of females. However, recent randomized studies of estrogen-progestins have not confirmed the presumed cardioprotective effect of these compounds when given to postmenopausal women^{8,9}. This suggests either a flaw in the mode, type and timing of hormonal replacement therapy, or that other yet poorly-explored areas of female physiology may confer strength against disease.

On the other hand, observational registry data suggest that women hospitalized for ST-elevation acute myocardial infarction fare worse than their male counterparts, even after adjusting for age, comorbidities, extent of epicardial coronary artery disease, left ventricular function at baseline, and treatment strategies¹⁰. Thus, although women relative to men enjoy a delay in the onset of ischemic heart disease and its complications, paradoxically more females than matched males with ST-elevation acute myocardial infarction appear to die in hospital. Whether this observation reflects true differences in biological processes or unidentified residual confounding factors still remains to be established.

To advance our understanding of gender-based differences in the manifestations of cardiovascular disease, this issue of the Journal inaugurates the first of two minisymposia dedicated to a sex-based comparison of the mechanisms, clinical presentation, and outcome of cardiovascular disease. The project was conceived by the Italian Society of Cardiology Working Group on Cardiovascular Diseases in Women. Its scope is to tackle some of several unsettled questions, namely: 1) do cardiovascular risk factors exert the same effect in male and female subjects; 2) can different neurohumoral mechanisms explain the lower incidence of sudden cardiac death among women; 3) what practical measures should cardiologists take to face the sex-based differences in clinical presentation, yield of invasive and non-invasive diagnostic tests, and natural history of disease; 4) last, but not least, do the available data allow definitive conclusions to be drawn on these matters, given that females have been largely under-represented in cardiovascular clinical trials.

We hope this is only the beginning of a far-reaching endeavor to better understand female cardiovascular pathophysiology, in order to recognize its distinctive features, take advantage of its strengths, and intervene more appropriately in the face of its possible frailties.

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